Version of Amended Claim With Markings to Show Changes Made:

9. (Amended) An isolated [A] host cell containing the vector of claim 8.

REMARKS

Applicants have studied the Office Action dated September 10, 2002 and have made an amendment to the claims. It is respectfully submitted that the application, as amended, is in condition for allowance. Reconsideration and allowance of the pending claims in view of the following remarks and above amendments is respectfully requested.

Rejection of claim 9 under 35 U.S.C. §101

The Examiner rejected claim 9 under 5 U.S.C. §101 because the claimed invention is not directed to statutory subject matter because claim 9 encompasses host cells as they occur in nature.

In response, Applicants have amended claim 9 as indicated above, to clarify that the claim is directed to isolated host cells.

Rejection of claims 4, 8-9, and 24-29 under 35 U.S.C. §101 and §112, 1st paragraph

The Examiner rejected claims 4, 8-9, and 24-29 under 35 U.S.C. §101 and §112, 1st paragraph, because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility and, consequently, one skilled in the art would not know how to use the claimed invention.

In making these rejections, the Examiner states, in particular, that the specification does not disclose any information regarding physiologic activity or functional characteristics of the protein encoded by the claimed nucleic acid, and that the state of the art is such that functional information can be automatically derived from structural information only to a limited extent (the Examiner cites Skolnick et al. to support this position). Therefore, the Examiner states that, since the specification does not provide an activity for the protein encoded by the claimed nucleic acid, one of ordinary skill in the art would not be able to predict what activity would be possessed by the protein of the instant application, and thus the invention is directed to a polynucleotide encoding a polypeptide of as yet undetermined function or biological significance. Therefore, the Examiner states that unless Applicants demonstrate that the claimed nucleic acid encodes a secreted transcobalamin II polypeptide, the physiological significance or the biological

role of the instant polynucleotide and the protein it encodes is as yet unknown and, therefore, the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility and, consequently, one skilled in the art would not know how to use the claimed invention.

Applicants respectfully traverse these rejections based on the following remarks.

Applicants agree with the Examiner that functional information can be derived from structural information only to a limited extent. Consequently, to accurately predict functional information from structural information, one must conduct multiple independent analyses and evaluate the results of these analyses collectively, rather than relying on a single type of structural analysis, such as relying only on BLAST homology. Accordingly, Applicants have collectively considered multiple analyses and lines of evidence, all of which consistently support Applicant's assertion that the protein of SEQ ID NO:3 functions as a transcobalamin II protein, and is therefore supported by patentable utilities that meet the requirements of 35 U.S.C. §101.

For example, the BLAST alignment provided on pages 1-2 of Figure 2 and the BLAST scores for the Top 10 BLAST hits provided on page 1 of Figure 1, indicate that the polypeptide of SEQ ID NO:3 shares a high degree of sequence homology with transcobalamin II. Even further support is provided by the fact that each of the top 7 BLAST hits, as indicated on page 1 of Figure 1, are all transcobalamin II proteins. Thus, Applicants have not relied on sequence identity between SEQ ID NO:3 and a single prior art sequence, or even a few prior art sequences, but at least all of the top 7 prior sequences that share the highest degree of sequence identity with SEQ ID NO:3. Importantly, no other proteins, other than transcobalamin II proteins, are amongst the top 7 BLAST hits, which clearly indicates that the skilled artisan would undoubtedly classify the polypeptide of SEQ ID NO:3 as a transcobalamin II protein. Furthermore, the proteins having the 8^{th}, 9^{th}, and 10^{th} highest BLAST scores, as shown on page 1 of Figure 1, are *Bos taurus* transcobalamin, *Rattus norvegicus* transcobalamin II precursor, and human transcobalamin I, respectively. Thus, all of the Top 10 BLAST hits are related to transcobalamin II, and no proteins other than transcobalamin-related proteins are within the Top 10 BLAST hits.

Additionally, Prosite analysis of functional domains and key regions is provided on page 1 of Figure 2. This Prosite analysis indicates the precise locations within SEQ ID NO:3 of the following structural elements: protein kinase C phosphorylation sites, casein kinase II phosphorylation sites, N-myristoylation sites, and an amidation site.

Also provided on page 1 of Figure 2 are SignalP results verifying that the polypeptide of SEQ ID NO:3 functions as a secreted protein.

Additionally, HMM analysis, provided on page 2 of Figure 4, provides further support for the functional classification of the polypeptide of SEQ ID NO:3 as that of a eukaryotic cobalamin-binding protein, with a score of 829.9.

In view of the above remarks, Applicants respectfully request that the Examiner collectively consider all the multiple analyses and evidence provided by Applicants in evaluating the function and utility of the polypeptide of SEQ ID NO:3 and the encoding nucleic acid molecules. All the available evidence collectively and consistently supports the functional classification of the polypeptide of SEQ ID NO:3 as that of a transcobalamin II protein. Consequently, one of ordinary skill in the would reasonably believe Applicant's assertion that the polypeptide of SEQ ID NO:3 is a transcobalamin II secreted protein, the utilities of which are well-established in the art and specifically asserted in the specification, particular on pages 3-5 of the specification, and especially at lines 10-16 of page 3, lines 22-31 of page 4, and lines 1-5 of page 5. Accordingly, Applicants respectfully request that the Examiner reconsider and remove the rejections of claims 4, 8-9, and 24-29 under 35 U.S.C. §101 and §112, 1st paragraph.

Conclusions

Claims 4, 8-9, and 24-29 are currently pending.

Claim 9 has been amended by way of the above amendment. The amendment to claim 9 adds no new subject matter and its entry is respectfully requested.

In view of the above amendment and remarks, Applicants respectfully submit that the application and claims are in condition for allowance, and request that the Examiner reconsider and withdraw the objections and rejections. If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is invited to call the undersigned agent at (240) 453-3812 should the Examiner believe a telephone interview would advance prosecution of the application.

Respectfully submitted,

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